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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,632	02/19/2002	Paul Habermann	P 30,612 USA	2603

23307 7590 02/17/2006

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,632	HABERMANN, PAUL	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005 and 25 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-14 and 21-33* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-14 and 21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/31/2005 has been entered.

[2] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[3] Claims 1-3, 7-14, and 21-33 are pending in the application.

[4] Applicant's amendments to the claims, filed on 5/31/2005 and 11/25/2005, acknowledged. The claim listing filed on 11/25/2005 replaces all prior versions and listings of the claims.

[5] Applicant's amendments to the specification, filed on 5/31/2005 and 11/25/2005, are acknowledged. The specification amendment filed on 5/31/2005 fails to satisfy the requirements of 37 CFR 1.121 for the reason(s) set forth in the 10/18/2005 Office communication. The specification amendment filed on 11/25/2005 has been entered into the application.

[6] Applicant's arguments filed on 5/31/2005 in response to the Office action mailed on 11/29/2004 have been fully considered and are deemed to be persuasive to

overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[7] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Restriction/Election

[8] Claim 3 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. While applicant argues "[c]laim 3 was withdrawn erroneously by the Examiner," this is not the case. A species election was set forth in the restriction requirement mailed on 2/24/2004. In the response filed on 3/23/2004, applicant elected the species of miniproinsulin, which reads on claim 2. In the Office action mailed on 5/20/2004, the examiner made the restriction requirement final and withdrew claim 3 from consideration. As claim 1, which is generic to the species of claims 2-3, was not found to be allowable, rejoinder of the species is not yet required. See MPEP 806.04(a).

In the instant response at p. 19, applicant argues that because the request for continued examination effectively withdraws the finality of the last Office action, the withdrawal of claim 3 should be rescinded. However, this is not found persuasive because generic claim 1, from which claim 3 depends, is rejected herein.

Because claim 3 is withdrawn, applicant is reminded to comply with the requirements of 37 CFR 1.121 and identify claim 3 as "(Withdrawn)" in the claim listing.

Claim Rejections - 35 USC § 112, Second Paragraph

[9] Claims 1-2, 7-14, and 21-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (claim(s) 7-14 and 21-28 dependent therefrom), 2 (claim(s) 31-32 dependent therefrom), 29-30, and 33 are indefinite in the recitation of "hirudin," "hirudin derivative," "natural hirudin isoform," "mini-proinsulin," and "lepirudin" as it is unclear from the claims and the specification as to those polypeptides that are considered to be encompassed by the terms "hirudin," "hirudin derivative," "natural hirudin isoform," "mini-proinsulin," and "lepirudin" such that a skilled artisan would recognize the intended scope of encoding nucleic acids. In this case, the specification fails to define which characteristics of a "hirudin," "hirudin derivative," "natural hirudin isoform," "mini-proinsulin," and "lepirudin" polypeptide are necessary to be included within the scope of the claims. Using hirudin as an example, it is well-known in the art that hirudin is a thrombin inhibitor. Thus, is any peptide or polypeptide that has the function of inhibiting thrombin considered to be a "hirudin" polypeptide? What characteristics of a "hirudin" polypeptide are considered necessary for a polypeptide to be included within the scope of the claims? Also, regarding the phrase "a hirudin derivative which is at least 40% homologous to a natural hirudin isoform," it is unclear as to the intended sequence(s) of a "natural hirudin isoform" such that a skilled artisan can make a determination of whether a "hirudin derivative" is 40% homologous (homologous is interpreted herein as

meaning identical) to a "natural hirudin isoform." It is suggested that applicant clarify the meanings of the above identified terms in the claims.

[10] RESPONSE TO ARGUMENT: Applicant argues the term "hirudin derivative" is definite in view of the amendment to claim 1 to define a "hirudin derivative" as being a protein that has at least 40% homology to a "natural hirudin isoform." This is not found persuasive because, as note above, it is not clear as to the scope of the intended sequence(s) that are considered to be a "natural hirudin isoform" such that a skilled artisan can make a determination of whether a "hirudin derivative" is 40% homologous to a "natural hirudin isoform."

Claim Rejections - 35 USC § 112, First Paragraph

[11] Claim(s) 1-2, 7-14, and 21-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Initially, it is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In this case, the examiner has broadly interpreted the phrase "a protein that is produced in and secreted by yeast" in claim 1 defining protein(Y) as any protein that can be produced and secreted by yeast, including endogenous and recombinantly produced proteins.

Claims 1 (claim(s) 7-14 and 21-28 dependent therefrom) are drawn to a genus of nucleic acid sequences having the formula as set forth in the claim. Claims 2 and 29-33 limit the components of the formula of claim 1.

The CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: "[i]n claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of nucleic acids, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the nucleic acid species within the genus from other nucleic acids such that one can visualize or recognize the identity of the members of the genus.

Also, for claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the

claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, as is the instant case, one must describe a sufficient variety of species to reflect the variation within the genus. The specification discloses only three species of the genus of claimed nucleic acid sequences, i.e., the nucleic acid sequences obtained in Examples 1-3 of the instant specification (specification at pp. 15-22). While it is noted that the specification describes the structures of additional representative species of signal sequences (represented by Sx in claim 1) at page 28, the specification fails to describe any additional representative species of the claimed genus of nucleic acid sequences, which encompasses species that are widely variant in structure and function. As such, the disclosure of the three representative species of nucleic acid sequences is insufficient to be representative of the attributes and features of all species encompassed by the recited genus of nucleic acid sequences.

Given the lack of description of a representative number of nucleic acid sequences, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[12] RESPONSE TO ARGUMENT: Applicant argues the specification discloses reduction to practice of nucleic acids in the Examples section and further discloses methods for using same. Applicant argues all members of the genus have the

identifying characteristic of "a sequence encoding hirudin or a derivative thereof and another protein." According to applicant, the reduction to practice of the specific Examples and the above-described identifying characteristic is sufficient to show applicant was in possession of the claimed invention.

Applicant's argument is not found persuasive. The examiner does not dispute applicant was in possession of the nucleic acid sequences obtained in Examples 1-3 of the instant specification (specification at pp. 15-22). Further, there is no dispute that all members of the genus must have Hir, which is defined in claim 1 as a nucleic acid encoding for hirudin or a derivative thereof and must have a protein(Y). What is at issue is whether the specification's disclosure of the nucleic acid sequences obtained in Examples 1-3 of the instant specification (specification at pp. 15-22) provides adequate written description of *all* species encompassed by the claimed genus of nucleic acids. As noted in previous Office actions, the genus of nucleic acids is widely variant, which is undisputed and even acknowledged by applicant (see particularly p. 7, middle of the 11/1/2004 Office action). As noted above, MPEP § 2163 states that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the disclosed species of Examples 1-3 fail to reflect the variation among the members of the genus, which encompasses species that are widely variant with respect to both structure and function. As such, the specification fails to adequately describe the claimed invention.

[13] Claims 1-2, 7-14, and 21-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid sequences prepared as described in Examples 1-3 of the specification and optionally having the signal sequences as set forth at page 28 of the specification, does not reasonably provide enablement for *all* nucleic acid sequences as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claim 1 broadly encompasses a nucleic acid having a sequence encoding *any* polypeptide considered to be a "hirudin" or a "hirudin derivative" that is at least 40% homologous to any "natural hirudin isoform" and having any function

and further comprising a sequence encoding any protein that is "produced in and secreted by yeast," which encompasses essentially any protein having any sequence and any function. Claim 2 limits protein(Y) of claim 1 to encoding miniproinsulin or a "derivative" thereof. The examiner has interpreted "derivative thereof" in claims 2, 29, and 30 as encompassing any protein. Claim 33 limits Hir to a "hirudin" polypeptide or a "lepirudin" polypeptide encoding sequence. The broad scope of claimed nucleic acid sequences is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of protein coding sequences including hirudin, hirudin-derivative, lepirudin, and mini-proinsulin encoding nucleic acids. In this case the disclosure is limited to those nucleic acid sequences prepared as described in Examples 1-3 of the specification and optionally having the signal sequences as set forth at page 28 of the specification.

The amount of direction provided by the inventor; The existence of working examples:

The specification discloses only three working examples of the claimed nucleic acid sequences, i.e., those three nucleic acid sequences prepared as described in Examples 1-3 of the specification. The specification provides further guidance for additional signal sequences that may be used to substitute the signal sequence in the nucleic acid sequences constructed according to Examples 1-3 in the specification (see page 28 of the specification). However, these working examples and guidance regarding additional signal sequences fail to provide the necessary guidance for making and using the entire scope of claimed nucleic acid sequences, including nucleic acids encoding non-functional polypeptides.

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: The amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within an encoding nucleic acid's sequence where modifications can be made with a reasonable expectation of success in obtaining an encoded polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Such is evidenced by the prior art, which teaches "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" ("Introduction to Protein Structure," Branden and Tooze, Garland Publishing Inc., New York, p. 247; cited in the 5/20/2004 Office action). Thus, a skilled artisan would recognize the high level of unpredictability that the entire scope of claimed nucleic acid sequences, including those

encoding hirudin derivatives and mini-proinsulin derivatives, would encode a polypeptide having the desired anticoagulant and insulin activities.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of generating variants of a nucleic acid, e.g., site-directed mutagenesis, are known, it is not routine in the art to screen for all nucleic acids having a substantial number of modifications encoding polypeptides having *any* structure and/or function, as encompassed by the instant claims.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the quantity of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

[14] RESPONSE TO ARGUMENT: Applicant argues working examples of nucleic acids encompassed by the claims and methods for using same. According to applicant, because the specification discloses at least one working example and a method for using it, the specification enables the full scope of claimed 6nucleic acids.

Applicants' argument is not found persuasive. In view of the analysis of the Factors of *In re Wands* as described above, it is the examiner's position that the disclosed three working examples fail to enable a skilled artisan to make and use all nucleic acids as encompassed by the claims without undue experimentation, particularly as these three working examples do not "bear[] a reasonable correlation to the entire scope of the claim."

Claim Rejections - 35 USC § 102

[15] Claim(s) 1, 7-14, 21, and 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Dawson et al. (US Patent 5,434,073; cited in the 5/20/2004 Office action). The claims are drawn to a nucleic acid sequence as set forth in claim 1, a vector or plasmid comprising said nucleic acid sequence, a host cell comprising said vector or plasmid, and methods for the production of a fusion protein.

Dawson et al. generally teach nucleic acids encoding hirudin fusion proteins. For example, Dawson et al. teach an expression vector encoding a hirudin-hirudin fusion protein comprising a galactose regulated promoter, a nucleotide sequence encoding an alpha-factor pro-peptide with a C-terminal sequence of Ser-Leu-Asp-Lys-Arg, an N-terminal hirudin, a Ile-Glu-Gly-Arg linker, a C-terminal hirudin or a C-terminal

streptokinase, and a yeast PGK terminator (See Example 1, columns 11-13 and Examples 8-9, columns 25-27). Dawson et al. teach expression of the hirudin-hirudin or hirudin-streptokinase fusion proteins by culturing Saccharomyces cerevisiae transformed with the expression vector, followed by isolation of the fusion protein (Example 2, columns 13-14 and Example 15, column 32). This anticipates claims 1, 7-14, 21, and 25-28 as written.

[16] RESPONSE TO ARGUMENT: Applicant argues that the SLDKR peptide sequence is not separate from the alpha-leader sequence, but is actually a part of it. According to applicant, none of the sequences of Dawson et al. contains a codon corresponding to component Z of the claimed nucleic acid.

Applicant's argument is not found persuasive. MPEP 2111 directs the examiner to give claims their broadest reasonable interpretation in light of the specification. In this case, there is no requirement in claim 1 or the specification that the nucleic acid of component Sx of claim 1 encode a "full" or "complete" signal sequence, only that Sx "is a nucleic acid encoding *a* signal sequence or leader sequence." In this case, the examiner has interpreted, in accordance with MPEP 2111, "a signal or leader sequence" as encompassing any fragment of an alpha-factor pro-peptide up to and excluding its C-terminal Arg that is capable of translocating a polypeptide as being "a signal or leader sequence." This interpretation is supported by the prior art reference of Rothblatt et al. (*EMBO J* 6:3455-3463), which teaches that deletions of the alpha-factor pro-peptide at the C-terminal end maintain the translocation function of a signal sequence (see particularly p. 3457, Figure 3). Therefore, when Bn is 0 and R is a

chemical bond, components Sx and Z are directly linked, and the Arg in the SLDKR sequence is considered to be component Z.

Claim Rejections - 35 USC § 103

[17] Claims 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dawson et al. in view of Badziong et al. (US Patent 5,095,092; cited in the 5/20/2004 Office action). Claim 22 limits the method of claim 21 to adjusting the pH to about 2.5 to 3.5 and isolating the fusion protein. Claim 24 further limits claim 21 to precipitating the fusion protein from the fermentation supernatant, releasing the protein encoded by protein(Y), and concentrating said protein by the recited methods.

Dawson et al. discloses the teachings as described above. Dawson et al. further teaches that following isolation of the hirudin-hirudin fusion protein, the fusion was cleaved, and the products analyzed by HPLC (column 15, Example 3). The method of fusion protein purification of Dawson et al. does not comprise the steps as set forth in claim 22 or 24.

Badziong et al. teach a method of purifying hirudin by adjusting the pH of S. cerevisiae culture filtrate to a pH of between 2 and 8, applying the pH-adjusted filtrate to a chromatography resin followed by eluting the hirudin from the resin (column 2). Badziong et al. teach that this method has advantages over other methods of purifying hirudin from yeast culture supernatants (column 1).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Dawson et al. and Badziong et al. to separate the culture

supernatant from the S. cerevisiae host cell and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. One would have been motivated to separate the culture supernatant from the S. cerevisiae host cell and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. because of the advantages of using the method of Badziong et al. for purifying hirudin from yeast culture supernatant. One would have a reasonable expectation of success for separating the culture supernatant from the S. cerevisiae host cell and purifying the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. because of the results of Dawson et al. and Badziong et al. Therefore, claims 22 and 24, drawn to methods for producing hirudin as described above, would have been obvious to one of ordinary skill in the art.

[18] Claim(s) 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dawson et al. in view of Badziong et al. as applied to claims 22 and 24 above and further in view of Mead et al. (US Patent 6,150,133). Claim 23 limits the method of claim 14 to cycles of separating the fermentation supernatant from the host cell and culturing the host cell in fresh medium, adjusting the pH to about 2.5 to 3.5, and isolating the fusion protein.

Dawson et al. and Badziong e al. disclose the teachings as described above. The combination of references does not teach a fermentation process as recited in claim 23 comprising cycles of separating the fermentation supernatant from the host cell and culturing the host cell in fresh medium.

Mead et al. teaches that in fermentation cultures of microorganisms, fermentation by-products, *e.g.,* acetate and ethanol, can have a toxic or inhibitory effect (column 1, top). Mead et al. teaches that the levels of such by-products in a fermentation medium for microorganisms including *S. cerevisiae* for heterologous secretion of a protein into a culture medium should be minimized (column 2).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Dawson et al., Badziong et al., and Mead to culture the host cell in a medium, separate the spent medium, and replace with fresh medium, separate the culture supernatant from the S. cerevisiae host cell and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. One would have been motivated to replace the medium and continue culturing with fresh medium in order to reduce the levels of toxic or inhibitory fermentation by-products and one would have been motivated to separate the culture supernatant from the S. cerevisiae host cell and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. because of the advantages of using the method of Badziong et al. for purifying hirudin from yeast culture supernatant as described by Badziong et al. One would have a reasonable expectation of success for separating the culture supernatant from the S. cerevisiae host cell, adding fresh medium to the host cells for continued culturing, and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. because of the results of Dawson et al., Badziong et al., and Mead et al. Therefore, claim 23, drawn to a method for producing hirudin as described above, would have been obvious to one of ordinary skill in the art.

[19] RESPONSE TO ARGUMENT: Applicant argues that because Dawson et al. does not disclose the claimed nucleic acid, by combining the teachings of Dawson et al. with the other cited references, one of ordinary skill in the art would not arrive at the claimed invention. Applicants' argument is not found persuasive.

Contrary to applicants' assertion, Dawson et al. anticipates the invention of claims 1, 7-14, 21, and 25-28, at least for the reasons stated above. Moreover, at the time of the invention, one of ordinary skill in the art would have recognized that Dawson et al. in combination with the other cited references would have rendered obvious the invention of claims 22-24 at the time of the invention.

Claim Rejections – Double Patenting

[20] The provisional double patenting rejections of claims 1-2 and 31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 4-5, and 25 of US non-provisional application 10/076,634 and claim 2 of US non-provisional application 10/076,631 is maintained. Due to amendment to the claims of this application and of the co-pending applications, the claims that are provisionally rejected have been updated.

RESPONSE TO ARGUMENT: Applicant argues the rejections are "merely provisional" and no response is required at the present time.

Conclusion

[21] Status of the claims:

- Claims 1-3, 7-14, and 21-33 are pending.
- Claim 3 is withdrawn from consideration.
- Claims 1-2, 7-14, and 21-33 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656